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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,702	04/15/2002	Camilo Anthony Leo Selwyn Colaco	8830-24	7592
23973 7590 02/10/2009 DRINKER BIDDLE & REATH ATTN: INTELLECTUAL PROPERTY GROUP ONE LOGAN SQUARE 18TH AND CHERRY STREETS PHILADELPHIA, PA 19103-6996				
			EXAMINER	
			GRASER, JENNIFER E	
			ART UNIT	PAPER NUMBER
			1645	
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			02/10/2009 PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/049,702

Applicant(s)COLACO, CAMILO ANTHONY
LEO SELWYN**Examiner**

Jennifer E. Graser

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11/28/08.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8-11 and 14-16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8-11 and 14-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date _____. |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____. | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/28/08 has been entered.

Claims 8-11 and 14-16 are currently pending and under examination.

The Examiner of Record has changed from Patricia Duffy to Jennifer Graser.

Claim Rejections - 35 USC § 112-2nd paragraph

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 8-11 and 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8-11 and 14-16 are drawn to compositions comprising a complex of any "induced stress protein" and "any antigenic peptide fragment". The mere recitation of a name, i.e., stress protein/antigenic peptide, to describe the invention is not sufficient to satisfy the Statute's requirement of adequately describing and setting forth the inventive concept. Further, the name "stress protein/antigenic peptide" is used for a vast number of different proteins in the prior art. The process in the product-by-process claims does

not serve to adequately define the claimed structure. The claim should provide any structural properties, such as the amino acid sequence of the protein or molecular weight, which would allow for one to identify the protein without ambiguity. The mere recitation of a name does not adequately define the claimed protein present in the claimed composition. It is noted that these claims are 'composition' claims and the structure being claimed is not adequately defined. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed.

.Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 8-11 and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Srivastava et al (WO 95/24923).

Srivastava et al disclose vaccines and compositions comprising stress protein-peptide complexes. They specifically teach heat shock proteins (HSP) may be used as

the stress protein. Srivastava et al define 'stress protein' as a protein whose intracellular concentration increases when exposed to stressful stimuli, is capable of binding to other proteins or peptides, and is capable of releasing the bound proteins in the presence of ATP or low pH. See page 10, lines 9-13. Srivastava et al define stressful stimuli to "include, but [are] not limited to, heat shock, nutrient deprivation, metabolic disruption, oxygen radicals, and infection with intracellular pathogens". See page 10, lines 13-15. Srivastava et al teach that they have discovered that a stress protein-peptide complex when isolated from a eukaryotic cell infected with a preselected intracellular pathogen and then administered to a mammal can stimulate a cytotoxic T cell response directed against cells infected with the same pathogen. See page 19, lines 1-9. Srivastava et al teach that the stress proteins can accumulate to very high levels in stressed cells, but they occur low to moderate levels in cells that have not been stressed. They give the example of Hsp70 which is hardly detectable at normal temperatures but becomes one of the most actively synthesized proteins in the cell upon heat shock and Hsp90 and Hsp60 are abundant at normal temperatures in almost all mammalian cells, but are even further induced at by heat. See bottom of page 23. Srivastava et al teach that their immunogenic stress protein-peptide complexes may include any complex containing a stress protein and a peptide that is capable of inducing an immune response in a mammal. See page 23, lines 20-27. The complexes can be prepared from cells infected with an intracellular pathogen as well as cells that have been transformed by an intracellular pathogen. See page 24, lines 5-10. Pages 46-48 teach that adjuvants and/or pharmaceutically carriers may be used. Page 13, lines 1-15 teach

that the complexes may be infected with bacterial, protozoal or parasitic intracellular organisms. Claim 15 specifically recites the 'stress' to be subjection to tumor necrosis factor. However, this is a product-by-process claim (as are all of the claims), "The patentability of a product does not depend upon its method of production. If the product in [a] product-by-process claim is the same as or obvious from a product of the prior art, [then] the claim is unpatentable even though the prior [art] product was made by a different process." *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. *In re Marosi*, 218 USPQ 289, 292 (Fed. Cir. 1983). There does not appear to be a structural difference between the product claimed and the product taught by the prior art, e.g., the claimed compositions solely comprise an immunogenic determinant any complex comprising a stress protein and an antigenic peptide fragment. *Srivastava et al* teach that their immunogenic stress protein-peptide complexes may include any complex containing a stress protein and a peptide that is capable of inducing an immune response in a mammal. See page 23, lines 20-27. *Srivastava et al* specifically teach the complexes can be prepared from cells infected with an intracellular pathogen as well as cells that have been transformed by an intracellular pathogen. See page 24, lines 5-10.

6. Claims 8-11 and 14-16 remain rejected under 35 U.S.C. 102(e) as being anticipated by Srivastava et al (US 5,961,979).

Srivastava teaches a vaccine composition comprising an immunogenic determinant comprising one or complexes between a shock protein and an antigenic peptide from the heat stressing of a cell infected with a bacterial, protozoal or parasitic intra-cellular pathogen (see title, abstract and claims). Srivastava teaches that a vaccine containing a stress protein peptide complex when isolated from cells infected with an intracellular pathogen and then administered to a mammal can effectively stimulate immune response against the pathogen (see column 4, line 60-68 summary of the invention). Srivastava teaches bacteria and protozoa (see column 7, lines 1-15). Srivastava teaches pharmaceutical carriers including aqueous composition and adjuvants (see column 23, lines 19-68). Srivastava teaches a method of producing the stress proteins including heat shock proteins and complex vaccine (see columns 5, 13 and 14). The prior art teaches the claimed invention. . Claim 15 specifically recites the 'stress' to be subjection to tumor necrosis factor. However, this is a product-by-process claim (as are all of the claims), "The patentability of a product does not depend upon its method of production. If the product in [a] product-by-process claim is the same as or obvious from a product of the prior art, [then] the claim is unpatentable even though the prior [art] product was made by a different process." In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward

with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 218 USPQ 289, 292 (Fed. Cir. 1983). There does not appear to be a structural difference between the product claimed and the product taught by the prior art, e.g., the claimed compositions solely comprise an immunogenic determinant any complex comprising a stress protein and an antigenic peptide fragment.

Response to applicant's arguments:

Applicants arguments are moot in view of the new grounds of rejection. However, Applicants arguments were drawn to a Srivastava patent from the same family so they will be addressed as they pertain to the new rejection. Applicants argue that TNF-induced cells showed a higher 20-200 fold higher antibody titer than those immunized with constitutively expressed heat shock proteins. These arguments have been fully and carefully considered, but are not commensurate in scope with the invention recited in claims 8-11, 14 and 16 which does not require the stress to be subjected to TNF. With respect to claim 15, the claim does not require a specific antibody induction or amount of complex present in the cell. The instant claims recite 'an immunogenic determinant comprising any induced stress protein and any antigenic peptide obtained from, a cell which has been infected with....'. Srivastava et al teach an immunogenic determinant comprising any induced stress protein and any antigenic peptide. The claims are product-by-process claims. "The patentability of a product does not depend upon its method of production. If the product in [a] product-by-process claim is the same as or obvious from a product of the prior art, [then] the claim is

unpatentable even though the prior [art] product was made by a different process." In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 218 USPQ 289, 292 (Fed. Cir. 1983). There does not appear to be a structural difference between the product claimed and the product taught by the prior art, e.g., the claimed compositions solely comprise an immunogenic determinant any complex comprising a stress protein and an antigenic peptide fragment. While a specific stressor may cause more stress protein and stress protein complexes to be induced, it does not appear to change the structure of the complex, nor does the claim require a specific level of complex.

Applicants further argue that there is an appreciable difference and distinction between the stress protein complexes derived by the process recited in the product-by-process claims when used to mediate an immune response and the constitutively expressed stress protein complexes by Srivastava which are "constitutively expressed stress protein complexes which are present in the non-stressed cells of Srivastava et al". They cite the teachings of Callahan et al 2002 and 2006 to support these statements. These arguments have been fully and carefully considered but are not deemed persuasive. Srivastava et al do not solely teach constitutively expressed complexes. Srivastava discloses the claimed compositions produced by a stress process and isolated from natural sources, produced in situ. The bacterial heat shock

protein (see Table 1 and definitions) is complexed together with an antigenic peptide fragment from a bacteria (see col. 7, line 7 "Chlamydia"), fungus, or protozoa, wherein the heat shock protein complex is isolated from natural sources (see col. 21, line 28).

Accordingly, Srivastava et al anticipates the claimed compositions.

7. Claims 8-11 and 14-16 are rejected under 35 U.S.C. 102(e) as being anticipated by Wallen et al (US 5,747,332).

Wallen et al teach methods for purifying and synthesizing heat shock protein complexes, in which heat shock proteins are associated with peptides, polypeptides, denatured proteins or antigens. See abstract and column 1, lines 63-66. The reference teaches that each of the heat shock protein complexes consists of a heat shock protein (HSP) that is bound tightly to an incomplete protein in a cell. See column 2, lines 38-43. Column 3, lines 49-67, teach that the heat shock proteins may be from prokaryotes, and include the GroEL/GroES complexes. Column 4, lines 2-4, teach that the complexes may be used as vaccines. The instant specification at page 6, line 20- page 7, line 5 specifically recites these protein complexes as emodiments. The passage recites :

The terms stress proteins and heat shock protein, as used herein, include those proteins that comprise the GroEL, GroES and DnaK and DnaJ families of bacterial HSPs and related families in other extra-cellular pathogens. These families are named on the basis of the size of the peptides which they encode. The families are highly conserved between species. In addition, many bacteria also express homologues of eucaryotic proteins. Preferably the vaccine contains a plurality of SP/antigenic peptide fragment complexes derived from the stressed pathogen. We particularly prefer that the GroEL, GroES, DnaK and DnaJ families of proteins are used as immunogenic determinants in the present invention, with DnaJ and GroEL most preferred. Preferably the SP complexes have greater than 25% homology and/or 20% identity at the amino acid level to the heat-induced HSP protein families.

Accordingly, Wallen et al anticipates the claims. The phrase "for eliciting an immune response" is an intended use only. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. With respect to the process recited in this product-by-process claims of the instant application, the HSP complex disclosed by Wallen is identical to one produced/isolated by these methods. With respect to claim 15, "The patentability of a product does not depend upon its method of production. If the product in [a] product-by-process claim is the same as or obvious from a product of the prior art, [then] the claim is unpatentable even though the prior [art] product was made by a different process." In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 218 USPQ 289, 292 (Fed. Cir. 1983).

8. Claims 8, 11 and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Laminet et al (EMBO Journal. 1990. 9(7): 2315-2319).

Laminet et al teach the isolated E.coli heat shock protein complex GroEL/ES. See abstract. The claimed compositions encompass a heat shock protein complex (comprising the HSP and associated peptide) from heat treatment of a bacterial

pathogen. The instant specification at page 6, line 20- page 7, line 5 specifically recites these protein complexes as emodiments. The passage recites :

The terms stress proteins and heat shock protein, as used herein, include those proteins that comprise the GroEL, GroES and DnaK and DnaJ families of bacterial HSPs and related families in other extra-cellular pathogens. These families are named on the basis of the size of the peptides which they encode. The families are highly conserved between species. In addition, many bacteria also express homologues of eucaryotic proteins. Preferably the vaccine contains a plurality of SP/antigenic peptide fragment complexes derived from the stressed pathogen. We particularly prefer that the GroEL, GroES, DnaK and DnaJ families of proteins are used as immunogenic determinants in the present invention, with DnaJ and GroEL most preferred. Preferably the SP complexes have greater than 25% homology and/or 20% identity at the amino acid level to the heat-induced HSP protein families.

Accordingly, Laminet et al anticipates the claims. The phrase "to elicit an immune response" is an intended use only. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. With respect to claim 15, the HSP complex disclosed by Laminet is identical to one produced/isolated by the method referred to in claim 11. "The patentability of a product does not depend upon its method of production. If the product in [a] product-by-process claim is the same as or obvious from a product of the prior art, [then] the claim is unpatentable even though the prior [art] product was made by a different process." In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference

between the claimed product and the prior art product. In re Marosi, 218 USPQ 289, 292 (Fed. Cir. 1983). GroEL/ES is a *heat-shock-protein* complex. A heat-shock protein by definition is a protein produced in response to stress, e.g., heat. This GroEL/ES complex is identical to the claimed composition.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thornton*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 8-11 and 14-16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10-14 and 17 of copending Application No. 10/049,704. Although the conflicting claims are not identical, they are not patentably distinct from each other because while the instant claims are drawn to a product-by-process claim in which the process recites an 'intracellular pathogen', as opposed to an 'extracellular pathogen' like the co-pending claims. The definition provided in the specification for these products encompasses 'extracellular

pathogens' within its definition of what can be considered 'intracellular'. For example, The instant specification at page 6, line 20- page 7, line 5 specifically recites these protein complexes as emodiments. The passage recites :

The terms stress proteins and heat shock protein, as used herein, include those proteins that comprise the GroEL, GroES and DnaK and DnaJ families of bacterial HSPs and related families in other extra-cellular pathogens. These families are named on the basis of the size of the peptides which they encode. The families are highly conserved between species. In addition, many bacteria also express homologues of eucaryotic proteins. Preferably the vaccine contains a plurality of SP/antigenic peptide fragment complexes derived from the stressed pathogen. We particularly prefer that the GroEL, GroES, DnaK and DnaJ families of proteins are used as immunogenic determinants in the present invention, with DnaJ and GroEL most preferred. Preferably the SP complexes have greater than 25% homology and/or 20% identity at the amino acid level to the heat-induced HSP protein families. .

Accordingly, the scope of the claims is not patentably distinct. The instantly pending claims do not recite that the stress proteins are produced by a "eukaryotic cell" as was previously argued. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1645 Fax number is 571-273-8300 which is able to receive transmissions 24 hours/day, 7 days/week.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Thursday from 8:00 AM-6:30 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi, can be reached on (571) 272-0956.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

/Jennifer E. Graser/
Primary Examiner, Art Unit 1645

2/4/09